

REMARKS

Foremost, Applicants thank the Examiner for the courtesies extended in granting the interview held on September 3, 2004 in which Applicants presented proposed claim amendments (draft claims 48-54) and a draft Declaration of Torben V. Borchert showing unexpected results supporting the non-obviousness of the claimed invention. The Examiner indicated that the declaration does appear to show sufficiently unexpected results to overcome the prior obviousness rejection over Suzuki et al. in view of Bisgaard-Frantzen et al. with respect to claims of a similar scope to the draft claims.

Pursuant to the interview, Claims 1-47 are cancelled and Claims 48-52 are added. Support for the subject matter set forth in Claims 48-52 is found in the specification as originally filed, including for example, the disclosures on page 10, third and fifth paragraphs (describing variants of *Bacillus stearothermophilus* and variants having at least 95% homology to SEQ ID NO:3), page 13, first and second paragraphs (describing the deletion of residues R179 and G180 in *Bacillus stearothermophilus* and SEQ ID NO:3), and page 15, lines 13-15 (describing substitutions of L349C and I428C in connection with *Bacillus stearothermophilus* and SEQ ID NO:3).

Accordingly, it is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments, the following remarks, and the Declaration of Torben Borchert under 37 C.F.R. 1.132 is requested.

I. The Rejection of Claims 30-33 under 35 U.S.C. 112, Written Description

Claims 30-33 were previously rejected under 35 U.S.C. 112, as lacking written description support. The Office states that this written description rejection can be overcome if claim 30 is amended to recite "wherein said variant has alpha-amylase activity, has at least 80%"

Applicants respectfully submit that this rejection is rendered moot by the new claims, as the new claims recite a homology of 95%. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 30-33, 35 and 37 under 35 U.S.C. 112, Enablement

Claims 30-33, 35 and 37 were previously rejected under 35 U.S.C. 112, as lacking enablement. The Office concluded that although these claims are enabled for alpha-amylase

variants having 90% homology to SEQ ID NO:3, that these claims lack enablement for alpha-amylase variants having 80% or 85% homology to SEQ ID NO:3.

Applicants respectfully submit that this rejection is rendered moot by the new claims as the new claims recite a homology of 95%. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 30-33, 35 and 37-39 under 35 U.S.C. 103(a) (Previously Withdrawn)

Claims 30-33, 35 and 37-39 were previously rejected in the Office Action of July 29, 2003 under 35 U.S.C. 103(a), as obvious over Suzuki et al. (JBC 260:6518, 1989) in view of Bisgaard-Frantzen et al., WO 95/10603, as follows:

Suzuki et al. teach a mutant *Bacillus amyloliquefaciens* α -amylase (BAA) with increased thermostability in which amino acid residues 176 and 177 (equivalent to residues 179 and 180 of SEQ ID NO:3) are deleted.

Bisgaard-Frantzen et al teach that the *Bacillus amyloliquefaciens*, *Bacillus stearothermophilus* and *Bacillus licheniformis* alpha amylases are homologous enzymes such that modification of corresponding residues in the three enzymes are expected to have similar effects. Bisgaard-Frantzen et al. further teach an alignment of amino acid sequences of the three enzymes which shows that positions 176 and 177 of BAA correspond to residues 179 and 180 of BST.

Therefore, it would have been obvious to one of ordinary skill in the art to introduce mutations disclosed by Suzuki et al. into the corresponding positions in *Bacillus stearothermophilus* α -amylase in order to produce a homologous α -amylase which would reasonably expected to have similar improved properties in view of the known homology between these α -amylases.

Even though there is no outstanding issue on obviousness, Applicants wish to establish on the record that new claims 48-52 are patentable over the prior art.

The presently claimed invention is directed to variants of *Bacillus stearothermophilus* alpha-amylase enzymes and to alpha-amylase variants having 95% homology to SEQ ID NO:3, and which contain deletions of amino acid residues R179 and G180. Applicants respectfully submit that the invention defined by Claims 48-52 would not have been obvious over the collective prior art teachings because it achieves substantially improved results with respect to thermal

stability, which at the time the claimed invention was made, would not have been expected by one of ordinary skill in the art.

In support of this position, Applicants submit herewith the Declaration of Torben V. Borchert Under 37 C.F.R. 1.132. As discussed at the interview, this declaration presents a comparison in thermostability between the following two pairs of alpha-amylase enzymes, namely, as the first pair:

- (a) *Bacillus amyloliquefaciens* alpha-amylase variant having a deletion of amino acids 176 and 177; and
 - (b) wild-type *Bacillus amyloliquefaciens* alpha-amylase;
- and, as the second pair,

- (c) *Bacillus stearothermophilus* alpha-amylase variant having a deletion of amino acids 179 and 180; and
- (d) wild-type *Bacillus stearothermophilus* alpha-amylase.

As explained in the Borchert Declaration, the improvement in thermostability in the *Bacillus stearothermophilus* alpha-amylase (BSG) resulting from the deletion of amino acids 179 and 180 was very substantial relative to the improvement in thermostability resulting from the deletion of amino acids 176 and 177 in the *Bacillus amyloliquefaciens* alpha-amylase (BAN), which is described Suzuki et al. In fact, the improvement in thermostability of the BSG variant (BSGdel) was between 5 and 6 times as great as the improvement in thermostability of the BAN variant (BANdel), i.e., a 63-fold improvement for BSGdel versus an 11-fold improvement for BANdel. As concluded by Dr. Borchert, these results were very surprising and unexpected in that they were significantly and substantially greater than what one of ordinary skill in the art would have expected, at the time the claimed invention was made, based on the collective teachings of the cited prior art.

In conclusion, the Borchert Declaration establishes unexpected results, and thus bolsters the non-obviousness of the invention as claimed. See *In re Soni*, 54 F.3d 746, 751, 34 USPQ2d (BNA) 1684, 1687 (Fed. Cir. 1995) (reversing the holding of the PTO Board of Patent Appeals and Interferences affirming the final rejection of claims for obviousness)("In our view, however, when an applicant demonstrates *substantially* improved results, as Soni did here, and states that the results were *unexpected*, this should suffice to establish unexpected results *in the absence of evidence to the contrary.*")(emphasis in original).


For the foregoing reasons, Applicants submit that the claims meet the requirements of novelty under 35 U.S.C. 102(b) and non-obviousness under 35 U.S.C. 103.

IV. Conclusion

In view of the above, It is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: September 6, 2004



Jason I. Garbell, Reg. No. 44,116
Novozymes North America, Inc.
500 Fifth Avenue, Suite 1600
New York, NY 10110
(212) 840-0097